Title: **Antiestrogens stimulate expression of transiently transfected and endogenous genes in rat pituitary tumor cell lines.**

Author(s): Larsen PR; Warne R

Author's Address: Howard Hughes Medical Institute Laboratory, Brigham and Women's Hospital, Boston, MA.

Source: Molecular and cellular endocrinology [Mol Cell Endocrinol] 1991 May; 77 (1-3), pp. 133-40.

Pub. Type: Journal Article

Language: English

Journal Info: *Country of Publication:* NETHERLANDS *NLM ID:* 7500844 *ISSN:* 0303-7207 *Subsets:* IM

MeSH Terms: Gene Expression/*drug effects
Pituitary Gland/*metabolism
Tamoxifen/*pharmacology
Animal; Blotting, Southern; Growth Hormone/genetics; Mutation; Pituitary Gland/cytology; Pituitary Gland/drug effects; Promoter Regions (Genetics); Rats; Transfection; Tumor Cells, Cultured

Abstract: Tamoxifen, *nafoxidine*, and clomiphene (1 x 10(-5) M) cause 5- to 15-fold increases in transient expression of plasmids transfected into rat somatomammotrophic pituitary tumor cell lines. To be effective, the antiestrogen must be present during the calcium phosphate transfection though it does not enhance the nuclear uptake or stability of transfected plasmid. The effect occurs with mammalian (rat *growth hormone*, mouse metallothionein I) or viral (thymidine kinase, Rous sarcoma virus) promoters and is inhibited by prior exposure of cells to high concentrations of estradiol but not glucocorticoid, progesterone or testosterone. Cis-tamoxifen, a conformation with much lower affinity for the estrogen receptor, has only one-fifth the effect of tamoxifen. Neither estradiol nor diethylstilbestrol have similar effects. Tamoxifen also increases endogenous rat *growth hormone* mRNA in these pituitary tumor cell lines. Transient expression in a number of other cell lines (JEG-3, COS-7, PC-12) is unaffected by tamoxifen suggesting the effect may be cell-type specific though MCF-7 cells are slightly responsive. The mechanism for the potent stimulation of gene transcription by these agents is not apparent but may be relevant to the mechanism of action of these agents as estrogen antagonists in vivo.

CAS Registry No.: 10540-29-1 (Tamoxifen)
9002-72-6 (*Growth Hormone*)

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Entry Date(s): *Date Created:* 19920630 *Date Completed:* 19920630

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09/736051

Title: **Toward a cure for *osteoporosis*: reversal of excessive bone fragility.**

Author(s): Turner CH

Author's Address: Center For Hard Tissue Research, Creighton University, Omaha, NE 68178.

Source: Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA [Osteoporos Int] 1991 Oct; 2 (1), pp. 12-9.

Pub. Type: Journal Article; Review; Review, Academic

Language: English

Journal Info: *Country of Publication:* ENGLAND *NLM ID:* 9100105 *ISSN:* 0937-941X *Subsets:* IM

MeSH Terms: Bone Remodeling/*drug effects
Osteoporosis/*drug therapy
Drug Therapy/trends; Forecasting; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Abstract: While *estrogen* replacement therapy and calcium supplementation appear to be effective at preventing postmenopausal *osteoporosis*, therapy for established *osteoporosis* is far less effective. The reduction of bone fragility should be a goal of a treatment for established *osteoporosis*. To this end, increases in cortical bone mass by subperiosteal new bone formation may produce the greatest mechanical advantage. Anti-resorptive drugs, such as etidronate, have shown potential for reducing the incidence of osteoporotic fracture in the short term, but their ability to produce a long-term benefit may be limited. An alternative approach might be to develop drug therapies that substantially increase cortical bone strength, namely by stimulating periosteal bone formation. Although sodium fluoride has proved to be problematic, there are several other potential *osteoporosis* therapies. They include treatment with anabolic hormones (e.g. *growth hormone* and anabolic steroids) and targeted delivery of *growth* factors. Also, anti-resorptive and formation-stimulating drugs might be combined in a new form of ADFR (coherence) therapy where the new acronym means: Activate-Depress-Formation stimulation-Repeat.

No. of References: 99

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